THE HEART IN SYPHILIS.[1]

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About one year ago I reported before the Society of the Alumni of the City Hospital a systematic anatomic study of the heart and aorta from fifty consecutive autopsies in cases of syphilis. I was stimulated to this investigation by the frequency with which I had observed serious and often fatal circulatory symptoms in cases of lues, many in patients who had been well treated and who not infrequently had long before ceased to manifest any signs or symptoms directly attributable to syphilis.

This study led me to believe that luetic involvement of the heart and aorta is much more frequent and much more serious in its direct effects than has been generally conceded by internists or even by syphilographers. In many text-books and monographs on this now newly understood infection, syphilis of the heart is not uncommonly mentioned as among the more unusual complications of the disease; yet in my postmortem series I find that 66 per cent. of my luetic cases, including well and incompletely treated instances, die as a result of or with serious circulatory disease apparently of specific origin. On analysis I find that in many reports this apparent infrequency of cardiac involvement is probably based on the relative rarity with which one finds true gumma in the heart at necropsy. In the other viscera the liver, the kidney, or brain, we also count as luetic the scleroses, fibroses, and degenerative changes which follow the more active syphilitic lesions.

Applying this same general basis for syphilitic cardiac lesions in my anatomic study of 50 cases, I found the following relative occurrence of definitely specific changes. The epicardium or visceral pericardium was diseased in 28 of the 50 instances. In regard to this membrane I call particular attention to a somewhat characteristic lesion manifested grossly by the appearance of opalescent patches of thickening which correspond to the perforation points of terminal arterioles. These opacities are formed of a mingled fibrous and endothelial hyperplasia which apparently occurs chiefly about the terminal arterioles. This lesion is not confined to lues but is much more frequent in it than in any other one condition which I have yet observed, and I have compared its genesis to that of syphilitic leukoplakia so frequently seen, especially in the buccal mucosa.

The myocardium was found diseased to a serious degree in 44 of the 50 cases, and true cardiac gumma was present in 5 instances, a percentage of occurrence closely approximating that given by Marcek. The most frequent myocardial change was found to be an inflammatory process manifested in the greater number of my cases, which were chiefly of late stage syphilis, by small round-celled infiltrations about the arterioles or by foci of fibrosis which I believe to be results of the inflammatory or infiltration process shown in the first-mentioned lesions. As a probable sequence of such changes, cardiac aneurysm was found present in 3 instances. Diffused or localized areas of scar formation were frequently encountered, but fibrosis was usually associated with other changes, often degenerative in character. Acute purely degenerative lesions were absent except in certain examples where they had apparently resulted from concomitant or independent disease.

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[1] Read before the Internal Section of the Buffalo Academy of Medicine, December 10, 1912.

In 35 instances disease of the coronary arteries was present to a relatively greater grade than the general arterial changes. This specific affinity to attack the coronary vessels has long been recognized, and in certain of my group of cases it was shown to have become an important factor even before the secondary rash had fully declared itself. The occurrence as well as the degree of coronary disease appears to correspond more or less with the activity rather than to depend on the duration of the infection. In this regard also it is interesting to note that age apparently plays little if any role in the determination of coronary disease in lues. Five of my most striking cases were below thirty years of age and 4 others below forty.

The type of the coronary change is variable. In 3 instances coronary thrombosis had resulted from an active primary endarteritis, but the most frequent change appears to be a fatty degeneration with endarteritis. From the diseased vessels there spreads out into the muscle all manner of changes, from a granulomatous and true myocarditis to fibrosis or necrosis, the result of deficient nourishment. In 2 examples of my autopsy series, aneurysm of the aortic arch was found present within six months after the primary lesion.

The natural questions which occur to a clinician after finding changes of this kind so prevalent are: When do they occur? Do they produce symptoms and signs which are clinically recognizable? May these lesions be prevented? May they be cured?

During the past two years my clinical studies have been largely directed toward an attempt to answer for myself these queries. Partly through the courtesy of my colleagues I have been able to carefully study in my own services a large group of cases of tertiary syphilis which directly applied to this subject and through the generosity of my colleague, Dr. J. A. Fordyce, of the syphilis service at the City Hospital, I have also been enabled to observe numerous cases of primary and secondary lues both before and after treatment.

It is manifestly impossible to go into accurate statistical or analytic details in so generalized a paper as this, but I hope to cover the ground of our studies in a sufficiently comprehensive manner to give a general idea of the conclusions which we have thus far reached. My associate, Dr. Carroll, and myself hope to publish later in considerable detail the various phases of the subject as they have appeared to us after a still wider and longer-continued experience along these lines.

As to the time when changes of a serious character appear in the heart. In many cases of aggressive onset during the secondary symptoms, irregularities of heart action appear; exercise, such as double time for sixty seconds, will frequently produce intermittence, extrasystoles, and other disturbances of rhythm. Abnormally rapid action is common and under stress; a soft systolic mitral murmur may appear. In brief the symptoms of heart deficiency at this stage are precisely such as at times appear in the febrile stage of most infections, such as typhoid, rheumatic fever, septicemia, and the like. One might fairly assume from this fact that the changes in these instances are precisely such as appear in any infection, and such I believe is the prevailing opinion. In a few instances, however, death has taken place, and autopsies have demonstrated these manifestations to be due to typical syphilitic inflammatory alterations in the heart muscle or in its arterioles. Three such cases have been studied by me.

In one case of my series which terminated unexpectedly before the secondary rash had fully appeared, and before the diagnosis had been made, death immediately resulted from a minute perforation of the wall of the aorta, just above the ring. A pronounced acute arteritis and periarteritis was found throughout the myocardium, particularly involving the vasovasorum of the aorta. Large foci of round-celled infiltration, with parenchymatous degeneration of the muscle cells and an active hyperplasia of the connective-tissue interstitium, was found—all typical and unmistakable syphilitic changes, yet they appeared in the early secondary stage of the disease.

Grassman records similar observations, and since I believe that I, with others, have demonstrated that these specific inflammatory changes develop first in and about the arterioles of the heart muscle, we cannot then assume other than that serious involvement of the heart may begin before or with the secondary stage of the disease. Obviously the postmortem evidence of this fact is not large, because cases now rarely die in this stage of the infection when nearly all patients are more or less effectively treated, one must therefore rely largely on clinical evidence for the confirmation of this fact.

Several cases in the active early secondaries which were seen by us in the service of Dr. Fordyce, and which showed unmistakable evidences of myocardial disease, such as tachycardia, extrasystoles, murmurs, and other irregularities of tone, rhythm, and force, when submitted to vigorous antisyphilitic treatment, showed within three days the disappearance of these signs, and all symptoms of cardiac disease vanished without resort to circulatory measures except rest in bed. Such cases, together with the postmortem evidence which I have been able to collect, satisfactorily indicate to me that early syphilitic lesions frequently appear in the heart, that they may be serious, and that they then cause symptoms of a sufficiently definite diagnostic character.

Now that the spirochetes of syphilis have been demonstrated in the heart muscle lesions of this type,[2] there remains no argument as to the specificity or significance of the lesions. It is inevitable that there should follow them changes of a more or less permanent and often grave nature.

If, as I believe my previous study has indicated, the changes in the heart chiefly originate in and about the bloodvessels, it is plain that the onset of the changes in the heart should occur early, for there can be no doubt but that we have an early septicemia or lymphemia in syphilis. Therefore it seems fair to assume that cardiac lesions are to be expected among the earliest of all visceral disease in this infection.

If we are then correct in this assumption, from the nature of the heart physiology, the largely unregenerative character of the heart muscle, and the inevitable fibrotic alterations which must succeed myocardial discrepancies, it follows that energetic treatment is imperative immediately after diagnosis in lues if for no other reason than because of the almost certainty of cardiac invasion. Fortunately it is no longer a question in therapeutics as to when treatment should be instituted in syphilis, and since this point has been satisfactorily settled, I have no doubt but that fewer cases of death as a result of luetic lesions of the heart will be reported.

As to the signs and symptoms which appear in syphilis as an indication of involvement of the heart, much work still remains to be done. As we have already remarked the most frequent and earliest lesions found are arterial or myocardial ones, and we all recognize the difficulty of absolute diagnosis of either of these conditions even when they are fully established—small wonder then that the early signs and symptoms of syphilitic involvement of the heart are neither clear, definite, nor characteristic.

Insofar as our personal observations go, the earlier symptoms are irregularity of action, more marked when strain is added, as by mild exercises or through nervous apprehension. Rapidity of action is also present in most cases, and it is incited to a degree and by conditions which in the normal would fail to elicit such a response. Pain and tenderness in the region of the heart demonstrated with or without heavy pressure over the precordium is present in a few of the early cases. I believe that these symptoms appear chiefly or only when extensive inflammatory lesions are present in the muscle or when dilatation has developed. I know, however, from clinical and postmortem evidence that pain and tenderness are not invariably present even in cases where actual cardiac aneurysm has developed. In no instances have I observed any significant alterations in the blood pressure except secondary modifications, when obvious decompensation was present, or in advanced cases when some such concomitant conditions as a nephritis complicated the picture. Neither have I observed any other characteristic alterations in the pulse in the early stages except the irregularity of rhythm and force already remarked. If I may be permitted to so express it, the characteristic of the irregularity of action in the early cases is its irregularity—its lack of system. I have never as yet observed anything indicative of a heart-block or auricular fibrillation in the early phases of the disease.

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[2] Buschke and Fisher, Deutsch. med. Woch., 1906, Nr. 19; Simmons, Münch. med. Woch., 1906, S. 1550.

In the latter stages of the condition, that is, in the tertiary and quaternary periods, the signs and symptoms of cardiac disease naturally become much more certain, though rarely in my opinion definitely indicative of lues—the signs and symptoms of the case become rather those of a myocarditis, of a cardiac aneurysm, of heart-block and the like. For this reason the specific etiology is likely to entirely escape detection. Symptoms and definite signs of cardiac disease may be absolutely absent, as shown in several instances which came unsuspected to autopsy when marked lesions were found. One cannot therefore assume that cardiac complications are necessarily absent in any case of syphilis because signs and symptoms are lacking.

Of the manifestations which appear with the greatest frequency in long-standing cases of lues, I believe that irregularity of action, especially when under strain or stress, is probably the most frequent, as it is also in the earlier stages. With the irregularity of action often appear murmurs or the accentuation of preëxisting murmurs or other alteration in their character. As we have already remarked in the early stages, murmurs are not very frequent, though they may appear; but in the long-standing cases they are frequent. Analysis of my postmortem cases shows a definite endocarditis present in 74 per cent.; 14 per cent. of the aortic ring; none of the mitral alone but 34 per cent. of both aortic and mitral. In many instances activity was still manifest, particularly in the aortic cases.

In advanced cases, as in the acute, pain in the region of the heart sometimes with tenderness is not infrequent; but here it is commonly of an anginal character, and reflected to either pectoral region, into the back, or down the arms. We have been able in most marked examples of this sign to satisfy ourselves that the symptoms of pain and tenderness were associated with dilatation, and is such as may occur in any type of myocardial degeneration after exercise. It is not infrequently entirely relieved by the administration of digitalis or strophanthus, and I am inclined to assume that in such cases pain is really caused by the dilatation, though this in turn may be due to coronary disease. I have seen several instances of undoubted angina pectoris, with or without dilatation, relieved by specific medication, and therefore consider them probably luetic in nature. None of these cases have come to autopsy, and are therefore not capable of absolute proof.

Stokes-Adams syndrome has been frequently reported as a result of syphilitic or gummatous myocarditis. During the past two years 5 of these cases, all history and Wassermann positive, have come to my notice, 2 in hospital and 3 in consultation with other physicians. Although in all these, tracings and in 2 electrocardiograms, also, showed the rhythm to be typical of heart-block, syncopal attacks have appeared in but 1. One hospital case, alternately under the service of Dr. Oppenheimer and myself, a man, aged seventy-eight years, has no disturbances whatever, but goes about the wards complaining of nothing except the natural disabilities of his age. It is important to record in relation to the role which lues plays in heart-block that these 5 cases have all been submitted to active antisyphilitic medication, but it has in no way altered the block, although in 2 cases the symptoms of dyspnea, cardiac pain, and of defective capillary circulation have been greatly relieved. So far as I have been able to ascertain no cases of heart-block have been recorded in the acute stages of syphilis. Several investigators record improvement under modern methods of treatment in late cases, such as mine, but we have not been thus fortunate.

It can safely be said that in the tertiary stages at least there are no definite pathognomonic signs or symptoms of syphilitic involvement of the heart. Diagnosis must in most instances rest on the discovery of a cardiac lesion, which is not accounted for otherwise, and a response to the Wassermann reaction. I do not wish to be misunderstood to indicate that I consider the Wassermann reaction infallible, either in a positive or negative sense, but I do consider it as yet the most definite sign in the diagnosis of syphilis in the later tertiary or quaternary stages, especially if the case has been more or less well, though incompletely treated.

In the diagnosis of heart involvement in syphilis a serious impediment is placed in our way in regard to history. According to my hospital statistics, based on confirmation by autopsy, only 30 per cent. gave a positive history. From my private records the percentage of positive history is here even less frequent. A certain number of these cases, more in private than in hospital practice, deny luetic history even when the truth would much better serve their purpose, and on the other hand, through lack of intelligence or observation, a considerable number of hospital patients overlook symptoms which would be observed by the more intelligent, and which when recited would definitely identify the condition.

Finally, I believe that the most definite and only certain criterion in a diagnostic way in cases of cardiac disease in lues is a betterment or cure of the conditions under purely specific medication. This has acted very satisfactorily with me in several instances of presumable syphilis, where the history and physical findings were doubtful and the Wassermann reaction inconclusive. To apply the therapeutic test in these cases does not appear any more unscientific to me than the administration of specific drugs in tumor of the brain, under the supposititious diagnosis of gumma when even the Wassermann is negative or indefinite.

While from the foregoing it must appear that the signs and symptoms of cardiac involvement in lues are indefinite, it will be granted that they are little more so than are those of most types of myocardial disease; but when signs and suggestive symptoms, especially with actual endocardial murmurs, appear without other likely cause, then the diagnosis either with or without the assistance of a history or a Wassermann reaction becomes quite sufficient. Several instances have appeared in my services in which the sudden, unexplained, and afebrile onset of an apparent aortic endocarditis has acted in a highly diagnostic way; in some such examples little opportunity for error exists.

Little need be said as to the progress of the involvement of the heart in lues once it has originated. The great frequency with which it terminated either fatally or in lesions which absolutely disqualify the patient from playing a normal part in the world's work is obvious to all who have considered the subject. Cases also exist with little or no disturbance even when extensive and serious lesions appear postmortem. We have found in our hospitals that a surprising number of cardiac cases in which the etiologic factors were obscure or entirely undiscovered, either responded to a Wassermann or on careful inquiry gave a history which justified the introduction of an antiluetic treatment, which was followed in a number of instances by such improvement that it could not be considered as otherwise than confirmatory. So general has been this result that we have frequently found it advisable to apply this therapeutic test even in cases historically and serologically negative.

As to the question whether the involvement of the heart may be prevented in lues. An absolute answer is at this time difficult, because a sufficient number of cases which received vigorous and protracted treatment in the early stages of the infection have not as yet remained sufficiently long under observation to justify definite conclusions in this respect. This much, however, must be admitted in the acute cases: That those in the active, aggressive, and progressive periods of the secondary stage which have been treated by modern methods have thus far shown no recognizable cardiac complications. Furthermore, as before stated in cases where cardiac lesions or symptoms had appeared and vigorous methods of treatment were applied, disappearance of these signs and symptoms has followed in most cases.

Unfortunately this is a line of work which it is unlikely that I shall be able to follow out because most of the cases which come to an internist are not in this period of infection, but are in the late tertiary stage. Perhaps I may, however, be pardoned for stating in this not inapt place my belief founded on my studies in pathologic anatomy that an attempt to divide syphilis into periods or stages is unsound pathologically and unsafe clinically —one commonly finds so-called tertiary lesions appearing in the secondary stages of the disease and from time to time in the tertiary period, sudden and aggressive exacerbations of the process spring up which can be only compared to those which we are accustomed to ascribe to the secondary stage. There is no essential difference, except in degree or size between the granulomatous processes of the secondary stage and the gummas of the third period.

It is a curious fact that although we have recognized since the days of Paré that syphilis caused disease of the heart, and that aortic disease in particular was frequently caused by it, we have apparently not appreciated until recently that these syphilitic manifestations should receive the same recognition and treatment which has in the past as in the present given such brilliant results in the treatment of syphilitic lesions elsewhere.

Collins and Sachs,[3] and Longcope, in 1910, called attention to the good results which follow the treatment of syphilitic lesions of the heart, just as like changes are managed when they appear elsewhere in the body. But few text-books as yet, however, point out the frequency of the complication or the necessity of adopting in it the same energetic line of treatment used in other forms of lues. Few practitioners apparently appreciate the results which may be reached by this means or the serious termination which is practically certain to follow in case no adequate treatment is instituted.

As an illustration of these features I wish to cite briefly the following case:

[3] Trans. Assoc. Amer. Phys., 1910.

Ten years ago a well-known colleague, in the course of his work, acquired a chancre in the end of the nose. Vigorous mercurial and iodine treatment had been promptly instituted under the supervision of an eminent syphilographer. Prompt disappearance of the obvious signs and symptoms of this disease took place, and the patient, himself an authority in this branch of work, continued the treatment for a period of two years, after which no evidences persisting, treatment was dropped. After a severe season of heavy work, early this past summer, he noticed that his heart intermitted, that some dyspnea was present on slight exertion, and an oppressive pain was almost constantly present in the region of the precordium. I found on examination that the heart was irregular, that the action became markedly intermittent on slight exertion, with the appearance of extrasystoles and of slight cyanosis and pallor. Auscultation showed the presence of a soft apical systolic murmur, not transmitted toward the axilla but upward over the sternum. A distinct systolic murmur was found at the aortic area transmitted into the vessels of the neck. The cardiac area was not increased, but heavy percussion over it caused discomfort. The Wassermann reaction was next day found strongly positive, but without waiting its determination the patient was the same day given 0.6 gram of salvarsan intravenously. A considerable reaction followed, and for several days the patient was seriously ill, with pains in the muscles and bones, high fever, and rapid pulse. Nonetheless, inside of one week the murmurs had decreased in intensity and the heart had become more regular and forceful in its action, and by the time that he was able to be about the cyanosis and dyspnea had vanished. Mercury was then administered and the patient has since remained under careful observation, though he is now able to continue his large practice. Two months later the intermittence had entirely disappeared, and after four months no heart murmurs can be found even after exertion.

As to the best methods of treatment. Although I do not feel that sufficient time has yet elapsed for me to draw definite conclusions from the cases which I have had under observation, certain facts have, however, come out which I believe may be of value to others, since some of them have been learned by me at the expense of considerable worry.

I may begin in this respect by the statement that so far as my experience goes the special type of treatment must be determined by the results on the patient—there is no other adequate measure. No two cases permit of identical methods. It is at present my chosen method of treatment to confine the patient to bed when the signs of cardiac disease are such as would suggest this step independent of the question of syphilis, but not otherwise. I believe that we have in the past been perhaps too frequent in our use of the bed in the treatment of all manner of circulatory disturbances. Many patients, especially young persons, do better if allowed up, with restrictions, of course, especially in the direction of excitement and exercise; entire suppression of muscular effort in my opinion is usually contraindicated.

If the indications of cardiac discrepancy demand it I give digitalis, morphine, strophanthus, or what other drug is apparently indicated by the condition and symptoms of the patient. In brief, I treat the case primarily as one of primary circulatory disease. I then begin the use of mercury, and my general preference is for the salicylate administered hypodermically in sterile albolene. I push this drug until definite but not poisonous indications of its effect are reached, afterward decreasing or intermitting its administration. In some cases mercurial inunctions appear more desirable, in other mercury by mouth; and I have at present a patient under my care who tolerates it only when administered in the old-fashioned vapors; speedy progress without discomfort having followed since this method has been adopted. I do not give the iodide in this period of the treatment, though I know no reason why it should not be so employed by those who have confidence in its specific action.

After the case has thus been under observation and treatment at least for a few days, in suitable instances, I recommend the use of salvarsan, not because I consider it indispensable, nor because I think it a more certain specific than mercury in the management of circulatory involvement in lues, but because given in the customary doses it has in most cases a more rapid effect than mercury alone. I believe that it affects some cases in which mercury seems inert, and also in the average patient I follow it up by the resumption of mercury.

In this form of syphilis, salvarsan is best administered intravenously. I have tried both methods, and my earlier preference was for the deep muscular injection. I am still of the opinion that this method may possibly give the most lasting effects in the disease, but that is not what I elect to use salvarsan for in the cardiac complications of lues, but for its quick effects and especially for its direct and speedy action on the bloodvessels and their immediately adjacent tissues. Added to this are the occasional foci of necrosis or abscess formation which may follow the intramuscular method even in the practice of the most careful technician, if he but continue the method long enough—a statement which a few months ago I might perhaps have questioned, but not so now. As to the special method of intravenous administration I have little to say; most of my cases have received the treatment from my associates, interested purely in syphilis, and I have therefore had cases managed by various technical methods. I have no preference for either the one or the other, and I believe that the best method is that with which the operator is himself most familiar.

At first I was accustomed to administer the full dose of 0.6 gram at one sitting; that is, for fully developed adults; following this up later by other doses if necessary, and by energetic after-treatment with mercury. Although I still maintain that theoretically this is the preferable method of treatment, acting on the basis of the theories in regard to its action, experience has shown that this is a dangerous procedure, and three cases so treated under my advice have nearly died as a result of the drug and its after-effects.

One of these cases which I saw with Dr. Wren I shall never forget. It was that of a small but previously vigorous man who had contracted his lues some twenty years before, and who had been treated at that time by the usual methods in vogue. He had since lived liberally in all respects, but without any apparent return of his syphilis. He had meanwhile acquired a family of three persons, and had carried on a large and important law practice.

When seen he was suffering from marked dyspnea, especially on slight exertion. Dilatation of the right and left ventricles was present. Both auricles were dilated. The heart action was irregular and intermittent at times; auricular fibrillation was perhaps present, though a satisfactory polygraph tracing could not be obtained. Most of the time he showed a typical heart-block, with periods of characteristic attacks of syncope. The recent history abounded with frequent seizures of this syndrome. I agreed in advising the use of salvarsan, and soon after the drug was given intravenously by a careful, experienced, and thoroughly reliable operator. Soon after the injection the ventricular contractions dropped to ten per minute; the patient became unconscious, went into collapse, and apparently became moribund. Only the most vigorous and persistent treatment saved his life, and he was for a long time thereafter gravely ill. The arsenic was in this case followed up by mercury, with relief of his cardiac distress and of most of the other signs and symptoms as well, but the heart-block has persisted. He has been able to resume his practice. No more salvarsan has been given, both because the doctors were not anxious to repeat their experience, and also because the patient absolutely refused to repeat the treatment, especially as he is now comfortable and apparently progressing under mercury and the iodides.

A further case illustrative not only of the dangers and benefits encountered in the treatment of cardiac syphilis by means of salvarsan and also of the manner in which the drug acts is probably worth recording in brief, particularly because of its characteristic history and the immediate bearing on the manner in which the drug affects the cardiac tissues in these cases.

The patient, a male, aged sixty-three years, entered my service at the City Hospital in February, 1910. He was a cook, formerly a soldier in the Prussian Army. He was married, but had had no children. He came of a healthy and long-lived family. His juvenile history was unimportant. He had rheumatism ten years previous to entering the hospital, and typhoid fever seven years ago. He was a moderate user of alcohol and tobacco. He denied not only the history of venereal infections, but also of all skin or mucous membrane symptoms which might be construed as of possibly syphilitic origin.

His chief complaint was of shortness of breath, especially on exertion. This symptom first gradually developed about one year before his entrance to the City Hospital, and was associated with pain in the precordium, headache, and swelling and cyanosis of the hands and feet. He lost between fifty and seventy pounds in weight during this time.

A summary of the chief points brought out by the physical examination were marked dyspnea on exertion, marked cyanosis of the face, hands, and feet, together with considerable edema of the hands and feet. The right pulse was small and indistinct, and was absent for most of the time. The left pulse was regular' the artery plainly palpable and thickened. The respiratory movements were shallow, rapid, and accompanied by sibilant rales, usually apparent even without direct auscultation.

The apex beat was visible and palpable in the fifth interspace, and four inches to the left of the midsternal line. The right cardiac border lay one and a half inches to the right of the midsternal line. The heart sounds varied greatly in rhythm, and in the occurrence, disappearance, and location of murmurs. The thorax presented considerable bulging and enlargement of the left side. Percussion demonstrated the presence of a broad area of dulness beneath the manubrium sterni, but no tracheal tug or abnormal suprasternal pulsations were found. There was enormous distention of the superficial thoracic veins which anastomosed below with the radicles of the superficial epigastrics. This venous anastomosis was especially definite on the left side of the body where the superficial veins of the arm and forearm were also much dilated.

The liver dulness was found to extend about a hand's breadth below the costal margin. The liver was firm on palpation, but somewhat tender. The spleen was enlarged, easily palpated, and tender. The abdomen contained considerable fluid.

Examination of the blood showed a constant polycythemia. The urine showed the continuous presence of albumin, casts, epithelial, and occasionally blood cells. The amount varied greatly, depending apparently on the condition of the circulation.

A diagnosis was made of aneurysm of the transverse arch, myocarditis, cirrhotic liver, and spleen, with secondary nephritis and polycythemia. Radiographs verified the diagnosis of aneurysm or aneurysmal dilatation of the transverse arch of the aorta, and because of the size of the sac, with its non-pulsatile character, it was assumed to be filled with laminated clot.

Syphilis was assumed to be present because of old skin lesions and the lack of other explanatory causes, but the Wassermann reaction was first reported negative, but later, after treatment had been instituted, it was several times found to be strongly positive.

Some relief was at first experienced from rest, the use of digitalis, and of the other usual cardiac drugs indicated in such cases; but he began to relapse as soon as he was allowed out of bed and about the ward. He developed from time to time hydrothorax, foci of bronchopneumonia, and attacks of pleurisy. Marked abdominal ascites and general edema appeared, and from time to time suppression of the urine, grave dyspnea, precordial pain, and other evidences of circulatory incompetence.

Mercurial medication was attempted first by mouth, then hypodermics of the salicylate, and finally, by inunction. These measures failed to give relief, and as he promptly developed under each early symptoms of mercurial poisoning attempts at treatment with this drug were suspended. Both massive and small doses of iodide of potassium were then prescribed, but he promptly developed a profuse pustular rash, began to run temperature, and this was also given up.

The patient was slowly becoming worse in every respect; the edema had become great, the urinary secretion small, and he passed into a comatose condition from which he could not be aroused by hot packs, cardiac stimulation, diuresis, and the other usual measures. Hitherto we had hesitated to give salvarsan because of the precarious condition of his circulation, fearing a Herxhimer reaction, which might terminate the picture. Finally, as death seemed to be but a few hours distant, it was determined to attempt the drug; 0.3 gram of old salvarsan was injected slowly into a superficial vein. The respiration stopped and he was thought to be dead. Venesection gave a sluggish flow of greatly cyanosed blood. Salt solution was injected intravenously, the extremities elevated and bandaged, adrenalin, camphor and ether, strychnine, and digitalin, were administered hypodermically, and the patient slowly rallied. The pulse became perceptible, the kidneys resumed secretion, the tremendous peripheral cyanosis was relieved, and in two days he was conscious. After fifteen days the patient was walking about the ward in tolerable comfort. No apparent change could be made out in the supposed aneurysm, but the polycythemia became much reduced, the pulse which had formerly presented extrasystoles, pulsus alternans, a jugular direct, and all manner of polygraphic curiosities became full and regular, though that on the right side remained small and at times imperceptible. Improvement was rapid during the summer months, so that the patient was able to walk about the hospital grounds; but attempts to resume mercurial medication always met with early toxic symptoms, and the old intolerance for iodides was still present. Digitalis now acted splendidly, as did also other cardiac stimulants, so that the circulation was maintained at a very satisfactory level.

The Wassermann reaction remained strongly positive, and this fall, as he ceased to gain ground, and urinary suppression, with symptoms of cardiac failure, again supervened, it was determined to repeat the salvarsan, though some difficulty was experienced in inducing the operator to undertake the second treatment; 0.2 gram was finally given intravenously, and again collapse occurred, but after vigorous management, with final recovery. Again marked improvement in the cardiac action and in the general strength of the patient took place. He was able once more to get about the hospital, and again became a tolerably comfortable ambulatory patient. Through the courtesy of my colleague, Dr. Potter, into whose service he had now passed, I was permitted to examine him. Apparently at this time, October, 1912, the retrosternal dulness had somewhat decreased in breadth.

In late November he developed a gangrene of the great toe of the right foot, preceded by great pain in this foot and leg. A diagnosis of embolism from a detached cardiac or aneurysmal clot was ventured. Death soon followed.

Through the courtesy of Dr. Larkin I am permitted to abstract the following data from the detailed protocol:

The retrosternal mass was found to be a widely dilated but not much sacculated arch, which together with the entire artery was extensively diseased and ulcerated, though most of the ulcerations were clearly in a healing and not progressive state. The walls of the aorta also presented marked longitudinal striations and folds which Dr. Larkin interpreted to indicate that shrinkage or contraction of the vessel was in progress. The heart was greatly enlarged. It showed a diffuse interstitial myocarditis, with occasional small gummatous scars clearly now largely healed, and undergoing rapid fibrosis. The general arteries were markedly diseased, but the coronary vessels were not extensively involved, and, as in the aorta, little calcification was present, for the process appeared to be essentially one of fibrosis and fatty degeneration. The small pulse on the right was explained by an old thrombosis, with a subsequent canalization of the right brachial artery.

The liver was greatly enlarged, and showed the results of chronic congestion, diffuse connective-tissue hyperplasia, and quite frequent healed gummatous scars. The spleen was much indurated and enlarged, no gummas could be made out in it. The kidneys showed a diffuse fibrosis, with nodules of compensatory parenchymatous hyperplasia.

The striking features revealed by the necropsy were the evidences of extensive disease of the aorta apparently undergoing healing and the presence of a syphilitic nephritis, hepatitis, and myocarditis, all well advanced in healing.

Realizing that microscopic study of these tissues might give a clue as to the manner with which healing may occur in the heart muscle in syphilitic myocarditis under the effects of salvarsan, such an examination was made. It seemed that this should be of special value, because in this case definite signs of improvement followed the use of the salvarsan, and little mercury or iodine was used. The changes therefore in such an instance would seem to be almost entirely due to the effects of the arsenic. The corroboration of the clinical benefit of treatment by direct anatomical evidence appears also to us of great importance.

MICROSCOPIC EXAMINATION. The muscle cells of the heart show in the main a considerable degree of atrophy, but with certain exceptions this atrophy appears to have been of pressure origin and not due to inherent disease of the muscle cells. For the greater part the striation is well preserved, a good many, however, show longitudinal striation, and there are many enlarged and karyokinetic nuclei, but cytoplasmic alterations are mostly wanting, except in the cells of the papillary muscles, where brown atrophy is quite general.

The connective-tissue interstitium is universally increased. This applies not only to the endomesium, but also to the connective tissue of the endocardium and epicardium. It is notably evident that hyperplastic connective tissue is most abundant and the evidences of recent growth most manifest about the arterioles of the coronary trunks.

Another peculiarity of this interstitial overgrowth is its highly cellular character, as though of rapid and rather recent formation. Cicatrization, or true scar formation, is not evident except in the papillary muscles and in the foci of old gummatous inflammation. Notwithstanding the fact that the connective tissue is so highly cellular, so apparently recently formed, few infiltrating leukocytes or wandering connective-tissue cells are present, and even about the blood channels which are crammed with red corpuscles few indications of active inflammation are to be made out. Lymphocytes are particularly few in number, both in the connective tissue and in the walls of the vessels, except again in the papillary muscles, where foci of infiltration and actively hyperplastic cells are present. Connective-tissue necrosis is also infrequent, but in the papillary muscles it is taking place, and degenerated foci of considerable size, marked by diffuse deposits of fatty and amorphous granules, are shown.

Notwithstanding the fact that the gross examination indicated that the coronary vessels were not markedly involved, the microscopic sections showed that the walls were much diseased. The muscle coats are largely disrupted and replaced by necrotic and fatty material, the elastica is so broken as to be hardly discoverable, and the intima is much roughened and eroded. As a general thing, the caliber of the vessels is enlarged. A striking feature is the absence of evidences of active infiltration or inflammation in the walls, such as would be marked, for example, by foci of round-celled infiltration or by active changes about the vasavasorum. The veins show marked atheromatous changes, similar though in lesser degree to those shown in the walls of the coronary arterioles. The venules and capillaries are generally surcharged with red corpuscles.

The scars found at various points in the heart walls, alike of the auricles and ventricles, and apparently representing the sites of old gummas, show under the microscope a replacement process of the muscle by a growth of young areolar tissue like that found elsewhere in the specimens. This tissue is strangely free from infiltrating or wandering cells and from marked cicatricial formation, and notwithstanding the apparently recent nature of this connective tissue and the presence of hyperemic vessels the blood trunks and their vicinity are surprisingly free from evidences of inflammatory reaction. There is nothing anywhere evident indicating activity of process and nothing now to signify that it is a syphilitic process.

Sections through the aortic wall show extensive atheroma, mostly without calcification, although numerous and large atheromatous cysts are present, together with considerable areas of necrosis. Many of the vasavasorum are surrounded by foci of infiltrating round cells, but the process in the intima and the subendothelial coats is definitely one of degeneration and not now of proliferation and progress. Attached to the intima are found numerous masses of clot, more or less organized. The whole process is definitely in a stage of healing, except perhaps about the vasavasorum.

Spirochetes could not be demonstrated in any of these sections.

Sections of other viscera showed almost universally similar changes.

The microscopic picture, so far as the heart is concerned, may be summarized as a fibroid myocarditis, singularly free from evidences of inflammation or cicatrization, except in the papillary muscles, where the disease lesions were all found most marked. The changes in the muscle cells are clearly secondary to those in the interstitium. Even in those places where scar formation extends entirely through the heart walls, inflammatory and cicatricial alterations are strangely few. The disease process apparently originated about the coronary vessels.

The changes are most advanced in the papillary muscles, and in those foci where gummas have apparently existed.

The picture of the entire process is one of definite and rapid healing, and one which is apparently taking place with the minimum injury to the surrounding parenchymatous tissues.

In a small group of tertiary cases we have employed neo-salvarsan in place of the older arsenical preparation. So far as we can determine we have received quite as good immediate results as with the older preparation, but of course, sufficient time has not yet elapsed to judge accurately as to this fact nor indeed as to the permanency of improvement under salvarsan. In a physician with long-standing lues now under observation, after a long course of hypodermics of mercury salicylate, one dose of neo-salvarsan was injected intramuscularly, with a striking improvement in heart action and the disappearance of an apical systolic murmur which had decreased but not disappeared under the mercury.

As to the use of the iodides in syphilis of the heart. I do not believe from my somewhat limited experience in acute secondary syphilis that this drug has any appreciable effect, and I am much inclined to believe with Collins and others, that the iodides have little really antisyphilitic or specific action. On the other hand, in tertiary cases, and particularly in such as show persistent evidences of heart-muscle infiltration, I have found in not a few instances that the iodides apparently do what neither salvarsan nor mercury does. Where irregularities, dyspnea, and a certain degree of cardiac distress have persisted after the arsenical-mercurial treatment, in these cases great relief has apparently followed from the employment of the iodides. I am myself not inclined to consider this as due to a specific action of the iodides since I have seen equal apparent benefit in cases of probably non-luetic myocardial disease, with negative Wassermann, negative history, and negative findings so far as syphilis is concerned. I believe that the iodides in these cases favor absorption of degenerative or inflammatory products, and so favor restitution of normal cardiac action.

In several cases under our observation not only has there been a marked improvement in heart action, apparently amounting to cure, but in some instances, as cited also by Collins and Sachs, there has been actual disappearance of a definite aortic murmur, supposedly due to an aortic endocarditis. But why should we wonder at the restitution of a sclerosed or ulcerated heart valve under syphilitic medication when we take as a matter of course the absorption of a gumma of the liver or brain under the same general treatment?

In a recent report before the Internal Section of the New York Academy of Medicine, Longcope records striking results from the arsenical treatment of syphilitic aortitis even in long-standing and advanced cases. Doubtless in Longcope's series of syphilitic aortitis many if not all his cases were complicated by myocardial lesions, and no doubt part of the benefit achieved in his aortic cases was due to betterment of myocardial lesions, just as beyond question some of the symptoms of my cases of syphilitic cardiac disease have been in part relieved through the effects of the drug on the aorta, there is no possible differentiation, of course, when it comes to judging the effects of treatment in either instance.

Adjuvant treatment, as though the cardiac lesions were not specific but idiopathic or general, is, of course, indicated. A few of my cases have taken the Nauheim treatment at home or in Nauheim with apparent benefit. Practically all of them have had digitalis or strophanthus at times as indicated. It goes without saying that all these circulatory measures should be employed as in other types of heart disorder, but the point which I wish to bring out in this paper and to emphatically emphasize is that they are secondary and relatively unimportant—the great essential is to treat these syphilitic lesions as syphilis.

As to the manner in which antisyphilitic medication cures or relieves lesions of the heart in syphilis, I have as yet little direct absolute evidence to offer, nor is it likely that I shall be able in the future to secure much material of conclusive character in this regard. The case just reported is perhaps as direct as can be expected. Inasmuch as I believe that I have demonstrated from previous studies that the characteristic and most important lesion in cardiac involvement is a gummatous process or an infiltration, a true syphilitic myocarditis, it seems logical to assume that benefit can be reached only by the local death of the spirochetes and by the subsequent absorption of the exudate and foreign tissue laid down in the myocardium as a result of the syphilitic infection. If, as seems indicated by the case just reported, this does take place, then it is easy to understand how improvement in heart action follows so promptly as we have found in many but not all the patients under our observation.

I have purposely made only a few references to the literature of the subject, but have confined myself to the data which I have collected and on which I have based my personal conclusions.

CONCLUSIONS. 1. Serious involvement of the heart is frequent in syphilis. Epicardium, endocardium, or myocardium or all together may be so diseased.

2. Cardiac involvement may develop early in the infection, though its symptoms may not be apparent until late.

3. The signs and symptoms are those of cardiac disorder, and little or nothing except the history, general aspects, and the Wassermann reaction may indicate the true etiology.

4. Treatment should be first along indicated circulatory lines, secondary as to time, but most productive and important of all it must be specific.

5. Good results, cures in many instances, will follow appropriate antisyphilitic treatment.

6. The special method of treatment should be individual, but both mercury and salvarsan are efficacious in the condition; usually they are preferably combined, in some instances the former, in others the latter acts best. Iodine is an efficient adjuvant in at least some instances.
7. Treatment should be continued until a permanent negative Wassermann is attained. Subsequent to this the management of the case should be along circulatory, not luetic lines.

SYPHILIS IN THE ETIOLOGY OF FIBROUS OSTEITIS.[1]

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Aside from the acute and chronic bacterial infections, tuberculosis and neoplasms of bone, there is a group of bone diseases of which leontiasis ossea, osteitis deformans, and osteomalacia are examples, whose stumbling nomenclature almost cries out for the light of etiology. It is for the purpose of suggesting the etiologic relationship between one of this group, osteitis fibrosa, or better, as termed by Bloodgood, chronic osteomyelitis fibrosa solida, and tardy hereditary syphilis that this communication is presented. The most recent contribution on this subject is by Elmslie[2] who states: "Beyond the opinion that fibrous osteitis is an inflammatory lesion, we must at present acknowledge that we know nothing of its pathology." In an exhaustive communication on this and kindred affections Bloodgood[3] says: "I, therefore, have been unable to find any definite etiologic factor, and I cannot agree with those who look upon the lesion as the result of trauma. . . . I agree with all the more recent investigators that the disease is an inflammatory one, in which the medullary tissue is replaced by a new formation of connective tissue with or without cyst formation." After reciting the history of my case, I shall endeavor to establish the premises upon which I conclude that this, if not many other similar cases, is due to syphilis of the late hereditary form.

Case I.—X. Y., male, farmer, aged twenty-two years, was referred to me in the Surgical Out-patient Department of the University Hospital by Dr. Charles C. Wolferth, of Clarksboro, N. J., January 2, 1912. His chief complaint was left-sided limp.

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[1] Read before the Pathological Society of Philadelphia, January 24, 1913.
[2] British Med. Jour., November 16, 1912, p. 1367.
[3] Annals of Surgery, 1910, lii, No. 2, 145.